REMARKS

Applicants respectfully request reconsideration of the present application in view of the foregoing amendments and in view of the reasons that follow. Applicants wish to thank the examiner for the interview granted with their attorney Matthew E. Mulkeen, Reg. No. 44,250. During this interview the outstanding claim rejections were discussed and are reflected by the contents of this response.

Claim 1 has been amended to include the recitations of claims 6 and 7. Support for this amendment can be found throughout the specification, *inter alia*, page 7, lines 13-17, page 3, line 25 to page 4, line 2, page 5, lines 24-29, page 15, line 13 to page 16, line 6, and Figure 2.

Priority Documents

As confirmed by the Notice of Acceptance dated March 4, 2004, the USPTO has received the priority document. The examiner, however, in the Office Action Summary, did not yet check the box indicating that the priority document has been received. Accordingly, acknowledgement of receipt of the certified copy of the priority document is respectfully requested in the next communication from the examiner. **This is applicants' second request for acknowledgement of receipt of the certified copies of the priority documents.**

Drawings

The examiner has not yet indicated in the Office Action Summary that the drawings filed with the original application papers on February 20, 2001 have been accepted. Acceptance of these drawings is respectfully requested in the next communication from the examiner. **This is applicants' second request for acceptance of the drawings.**

Rejections Under 35 USC § 112, First Paragraph, Enablement

The claims have been amended to overcome the rejection for lack of enablement.

Rejection Under 35 USC § 103(c), Obviousness

Claims 1 and 6-7 stand rejected as being obvious over Lemoli et al (Blood, 1991) in view of Kiyoi et al (Leukemia, 1998), Yokota et al (Leukemia, 1997, 11: 1605-1609, IDS item) and Carow (Blood, 1996). Claims 1 and 9 are rejected over Lemoli et al (Blood, 1991) in view of Kiyoi et al (Leukemia, 1998), Yokota et al (Leukemia, 1997, 11: 1605-1609, IDS item) and Carow (Blood, 1996), in view of Li (PNAS, 1992) and Nakao (Leukemia, 1996).

With respect to Lemoli et al, as explained in detail in the previous response to the anticipation rejection, they merely evaluated tumor-killing activity (tumore-lytic activity) known purging agents to remove tumor cells (AML cells) contaminated in human bone marrow cells collected from AML patient, of which tumor (AML)-killing mechanism is completely irrelevant to the expression of FLT3/ITD in the tumor cells because, inconsistent with the findings by Teller et al or Kiyoi et al of the record that only 20% of AML cells express FLT3/ITD mutant, Figure 2 of Lemoli et al show more than 90% AML cells were killed by single or, in combination, purging agent(s), which means the tumor (AML)-kiling mechanism by purging agents of Lemoli et al is irrelevant to the FLT3/ITD expression of 20% of AML cells, whereas the present invention relates to the method to identify a compound which inhibit a proliferation of FLT3/ITD-expressing tumor cells (AML or MDS cells as amended) by inhibiting FLT3/ITD function. In addition, it should be noted that "killing" of tumor cells and "inhibition" of them is different phenomenon or parameter. The compounds that Lemoli et al intended to identify are tumor-killing compounds to remove tumor cells contaminated in bone marrow cells to be autologously transplanted to the AML patient, whereas the present invention provides a method to identify a compound that which inhibit a proliferation of FLT3/ITD-expressing tumor cells (AML or MDS cells as amended) by inhibiting FLT3/ITD function.

As described in the present application (on page 3, line 25 to page 4, line 2; page 5, lines 24 to 29; page 15, line 13 to page 16, line 6, and Figure 2), one of the noteworthy features of the present invention is that the inventors of the present invention found that

primary blood cells or hematopoietic stem cells require IL-3 for their proliferation, whereas the blood cells or hematopoietic stem cells which have been prepared to express FLT3/ITD mutant is capable of proliferate in the absence of IL-3, in other words, they can proliferate IL-3 independently. Based on these findings, as recited in steps (a) and (b) of claim 1, (i) providing blood cells or hematopoietic stem cells which express FLT3/ITD and proliferate IL-3 independently, and then (ii) contacting the FLT3/ITD-expressing cells with candidate compound in the absence of IL-3, the present invention can identify compounds which can inhibit the proliferation of specifically FLT3/ITD-expressing tumor cells.

As described in the present application (on page 3, line 25 to page 4), the IL-3-independent proliferation is likely induced by proliferative signaling of FLT3/ITD and thus this proliferation is responsible for progression of tumors in hematopoietic organs such as AML (acute myeloid leukemia). Accordingly, a method of the present invention, which allows identification a compound that is capable of inhibiting proliferation of specifically FLT3/ITD-expressing tumor cells is one of the unexpected advantageous effects of the present invention.

Neither Lemoli et al nor all the other references, Kiyoi et al, Yokota et al, Li at al and Nakao et al disclose or suggest the inventive features of the present invention. The examiner has stated that the Yokota reference "strongly suggests that the abnormal protein product derived from this mutation functions dominantly and increases the growth of leukemic cell[s]." Applicants contend that the suggestion of Yokota is not sufficient to establish a *prima facie* case of obviousness. Rather this is an invitation to engage in further research, which is improperly basing an obviousness rejection on what a person of ordinary skill in the art might try or find obvious to try. As the Federal Circuit and the CCPA have held, this standard is incorrect when making a determination of obviousness. The proper standard is what the prior art would have lead the skilled person to do. See *In re Dow Chemical v. American Cyanamid Co.*, 837 F.2d 469, 471 (Fed. Cir. 1988) and *In re Thomlinson*, 363 F.2d 928, (CCPA 1966) None of the other cited references overcome this deficiency of Yokota.

Conclusion

Applicants believe that the present application is now in condition for allowance. Favorable reconsideration of the application as amended is respectfully requested. The examiner is invited to contact the undersigned by telephone if it is felt that a telephone interview would advance the prosecution of the present application.

The Commissioner is hereby authorized to charge any additional fees which may be required regarding this application under 37 C.F.R. §§ 1.16-1.17, or credit any overpayment, to Deposit Account No. 19-0741. Should no proper payment be enclosed herewith, as by a check or credit card payment form being in the wrong amount, unsigned, post-dated, otherwise improper or informal or even entirely missing, the Commissioner is authorized to charge the unpaid amount to Deposit Account No. 19-0741. If any extensions of time are needed for timely acceptance of papers submitted herewith, Applicants hereby petition for such extension under 37 C.F.R. §1.136 and authorizes payment of any such extensions fees to Deposit Account No. 19-0741.

Respectfully submitted,

Date March 27, 2006

By _____

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